

Filed: January 8, 2002

Inventors: O'Harte *et al.*

Amendment and Reply

Page 2

The following Listing of the Claims will replace all prior versions and all prior listings of the claims in the present application:

Listing of The Claims:

1. (Currently amended): A peptide analogue of GIP (1-42) comprising at least 15 amino acid residues from the N terminal end of GIP (1-42), the analogue containing Tyr¹ glucitol GIP (1-42) and having at least one additional amino acid substitution or modification at positions 2-3 position 1-3 not including Tyr¹ glucitol GIP (1-42).
2. (Currently amended): A peptide analogue as claimed in claim 1 or 20 or 21 or 22, including modification by fatty acid addition at an epsilon amino group of at least one lysine residue.
3. (Original): A peptide analogue of biologically active GIP (1-42) wherein the analogue is Tyr¹ glucitol GIP (1-42) modified by fatty acid addition at an epsilon amino group of at least one lysine residue.
4. (Currently amended): A peptide analogue as claimed in claim 1 or 20 or 21 or 22, wherein the further comprising at least one additional amino acid modification is chosen from the group consisting of D-amino acid substitution in position 1, D-amino acid substitution in position 2, D-amino acid substitution in position 3, N terminal glycation, N terminal alkylation, N terminal acetylation and N terminal acylation (a) D-amino acid substitutions in 1, 2 and/or 3 positions and/or (b) N terminal glycation, alkylation, acetylations or acylation.
5. (Currently amended): A peptide analogue as claimed in claim 1 or 20 or 21 or 22, further comprising an additional substitution consisting of the amino acid in the 2

Filed: January 8, 2002

Inventors: O'Harte *et al.*

Amendment and Reply

Page 3

or 3 position being substituted by lysine, serine, 4-amino butyric acid, Aib, D-alanine, Sarcosine or Proline.

6. (Currently amended): An analogue as claimed in claim 1 or 20 or 21 or 22, further comprising an additional modification of the N terminus, wherein the modification is glycation, alkylation, acetylation or the addition of an isopropyl group.
7. (Canceled)
8. (Currently amended): A pharmaceutical composition including an analogue as claimed in claim 1 or 20 or 21 or 22.
9. (Original): A pharmaceutical composition as claimed in claim 8 in admixture with a pharmaceutically acceptable excipient.
10. (Previously presented): A method of N-terminally modifying GIP or analogues thereof the method comprising the steps of (a) synthesizing a GIP peptide from the C-terminal to the penultimate N terminal amino acid, (b) providing tyrosine as a F-moc protected Tyr(tBu)-Wang resin, deprotecting the N-terminus of the tyrosine and reacting with modifying agent, allowing the reaction to proceed to completion, cleaving the modified tyrosine from the Wang resin to produce a free modified tyrosine and (c) adding the free modified tyrosine to the N terminus of the synthesized peptide of (a).
11. (Currently amended): A method as claimed in claim 10 wherein the modifying agent is chosen from the group consisting of: glucose, acetic anhydride and and/or pyroglutamic acid.

Filed: January 8, 2002

Inventors: O'Harte *et al.*

Amendment and Reply

Page 4

12. (Currently amended): A method for treating diabetes comprising administering to an individual in need of such treatment an effective amount of an analogue analog according to claim 1 or 20 or 21 or 22.
13. (Currently amended): A peptide analogue of GIP (1-42) comprising at least 15 amino acid residues from the N terminal end of GIP (1-42), the analogue containing Tyr¹ glucitol GIP(1-42) and having at least one additional amino acid substitution or modification at positions 2-3 position 1-3 in addition to Tyr¹ glucitol GIP (1-42), and including modification by fatty acid addition at an epsilon amino group of at least one lysine residue.
14. (Currently amended): A peptide analogue as claimed in claim 3, further comprising at least one additional modification chosen from the group consisting of D-amino acid substitution in position 1, D-amino acid substitution in position 2, D-amino acid substitution in position 3, N terminal glycation, N terminal alkylation, N terminal acetylation and N terminal acylation (a) D-amino acid substitutions in 1, 2 and/or 3 positions, and (b) N terminal glycation, alkylation, acetylation or acylation.
15. (Previously presented): A peptide analogue as claimed in claim 3, further comprising an additional substitution consisting of the amino acid in the 2 or 3 position being substituted by lysine, serine, 4-amino butyric acid, Aib, D-alanine, Sarcosine or Proline.
16. (Previously presented): An analogue as claimed in claim 3, further comprising an additional modification of the N terminus, wherein the modification is chosen from the group consisting of: glycation, alkylation, acetylation and the addition of an isopropyl group.

Filed: January 8, 2002

Inventors: O'Harte *et al.*

Amendment and Reply

Page 5

17. (Currently amended): A pharmaceutical composition including an analogue as claimed in claim 2 or 3.
18. (Previously presented): A pharmaceutical composition as claimed in claim 17 in admixture with a pharmaceutically acceptable excipient.
19. (Currently amended): A method for treating diabetes comprising administering to an individual in need of such treatment an effective amount of an analogue analog according to claim 2 or 3.
20. (New): A peptide analogue of GIP (1-42) comprising at least 15 amino acid residues from the N terminal end of GIP (1-42), the analogue containing D-Tyr¹ amino acid substitution in position 1, or N terminal alkylation, or N terminal acetylation or N terminal acylation.
21. (New): A peptide analogue of GIP (1-42) comprising at least 15 amino acid residues from the N terminal end of GIP (1-42), the analogue containing D-Tyr¹ amino acid substitution in position 1, or N terminal alkylation, or N terminal acetylation or N terminal acylation, having at least one additional amino acid substitution or modification at positions 1-3.
22. (New): A peptide analogue of GIP (1-42) comprising at least 15 amino acid residues from the N terminal end of GIP (1-42), the analogue containing at least one amino acid substitution or modification at positions 1-3.